Pattern Of Occult Lymph Nodal Metastasis To The Neck In Early Carcinoma Tongue With Clinically Negative Neck Nodal Status In Patients Of Indian Origin Presenting To A Tertiary Hospital.

A dissertation submitted to the Dr. M.G.R. Medical University, Tamil Nadu, in partial fulfillment of the requirement for the M.S. branch I (General Surgery) examination to be held in March 2009.

Certificate

This is to certify that the topic entitled "**The pattern of occult lymph nodal metastasis to the neck in early carcinoma tongue with clinically negative neck nodal status in patients of Indian origin presenting to a tertiary hospital"** is a bonafide work done by Dr. Anshika Mittal, post graduate in General Surgery of Christian Medical College, Vellore. This work has been carried under my guidance and supervision in partial fulfillment of the regulation of Dr. M.G.R. Medical University of Tamil Nadu for Master of Surgery- Branch I (General Surgery) examination to be held in March 2009.

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ABSTRACT

A descriptive study was conducted in the department of General Surgery at CMC-Vellore. A total of 30 patients, who were diagnosed to have early carcinoma tongue (T_{1-2} N_0 M_0) between July 2006 and August 2008, underwent wide local excision of the primary lesion and either modified radical neck dissection or radical neck dissection. Out of these 30 patients, 7(23.3%) were found to have occult metastasis to the neck lymph nodes. All of these nodal metastases were limited to the levels I,II and III lymph node groups. A univariant analysis of primary tumor histopathological characteristics revealed that the presence of perineural invasion, angiolymphatic invasion or an invasive growing front are factors significantly related to the presence of occult lymph nodal metastasis. As there is significant morbidity associated with modified radical neck dissection, a selective neck dissection (Levels I,II and III) may be an appropriate operation for early carcinoma tongue (T_{1-2} N_0 M_0).

HYPOTHESIS, AIMS AND OBJECTIVES

HYPOTHESIS:

-- A "comprehensive" (modified neck dissection III) neck dissection is not warranted in patients with clinically T_{1-2} N_0 M_0 carcinoma tongue in the context of patients of Indian origin.

-- There is a relationship between the primary tumor characteristics and the pattern of occult neck nodal metastasis.

AIMS AND OBJECTIVES:

Primary Objective

To determine the presence and pattern of occult metastasis at the various levels of neck lymph nodes in patients with T_{1-2} carcinoma tongue with clinically negative neck.

Secondary Objective

A) To describe, if any, the relationship of the pattern of lymph node metastasis with respect to the following-

i) Exact location of the primary tumor

ii) Grade of the tumor

iii) Tumor depth

iv) Depth of muscle invasion

v) Invasive or pushing front

vi) Perineural invasion

vii) Angiolymphatic invasion

B) To describe the morbidity associated with the neck dissection in these patients

INTRODUCTION

Perhaps there is no greater controversy in head and neck cancer than the proper treatment of the N_0 neck in squamous cell carcinoma tongue. The options of modified radical dissection and selective neck dissection exist for management of early carcinoma tongue.

There are factors related to the primary tumor which may be able to predict lymph node metastasis. Presence of such factors may affect management of a clinically negative neck.

It is well known that this cancer is a locally aggressive disease that can cause great morbidity and mortality because of the inherent complexity of the tongue and physiologic functions that take place (taste, speech, and deglutition) (Pillsbury 1997). The appropriate management of the primary tumor and the secondaries in the neck nodes is therefore necessary.

REVIEW OF LITERATURE

Epidemiology

Squamous cell carcinoma of the tongue is relatively common in India and forms a significant group of all the Head and Neck Malignancies as per statistics collected in Bombay (Jayant K 1977). Oral carcinoma is the commonest cancer among the males and the second most common cancer in females. Carcinoma of the tongue comprises of 3% of all malignancies and 30% of oral malignancies in India (Kazi 2003). Cancer of the oral cavity and pharynx is ranked as the 7th most common cancer among men in the U.S., with an incidence rate of 16.7 per 100,000(Shiboski, Schmidt et al. 2005). It is the fourth most common cancer and ranked tenth among the most common causes of death among African American men in U.S.

The incidence of metastasis to neck nodes was found to be dependant on the T staging of the primary tumor -- in a study by Lindberg et allT_1(14%), T_2(30%), T_3(47.5%), T_4(76.5%)(Lindberg 1972). In another study by Beyer et all T_{1-2} (18.6%), T_{3-4} (31.6%) (Byers 1986).

Surgical Anatomy

Tongue

Oral tongue is defined as the anterior 2/3rd of the tongue bounded posteriorly by the circumvallate papille. The anatomy of tongue muscles are shown on the right. These muscles are divided into extrinsic (originating outside the tongue) and intrinsic (situated within the tongue) muscles. The four major extrinsic muscles of the tongue are mylohyoid, hypoglossus, styloglossus and genioglossus muscles. The intrinsic muscles being superior longitudinal muscle, inferior longitudinal muscle, verticalis muscle and transversalis muscle.

Three fourth of the cases of oral cavity cancer involve only 10% of the area of the oral cavity, believed to be secondary to the pooling of carcinogen-laden saliva. This area extends from the anterior floor of the mouth along the mandible gingivobuccal sulci, including the ventrolateral aspect of the tongue, to the retromolar trigone and the anterior tonsillar pillars (Pillsbury 1997).

Neck

The various levels of neck nodes are defined as follows --

Lymph node level	Description
Level I	IA (submental): LNs within triangular boundary of anterior belly of digastric muscles and the hyoid bone. IB (submandibular): LNs within the boundaries of the anterior belly of the diagastric muscle, stylohyoid muscle and the body of mandible.
Level II	LNs from the skull base to inferior border of the hyoid bone,

	anterior boundary being stylohyoid muscle and posterior boundary posterior border of sternocleidomastoid muscle. IIA: LNs anterior to the spinal accessory nerve IIB: LNs posterior to the spinal accessory nerve.
Level III	LNs from the inferior border of the hyoid bone to the inferior border of the cricoid cartilage.
Level IV	LNs from the inferior border of the cricoid cartilage to the clavicle below .
Level V	LNs with triangle formed by- apex formed by stermastoid and trapezius muscle , inferiorly the clavicle, anteriorly the posterior border of sternomastoid muscle, posteriorly trapezius muscle.

Staging and prognosis

Carcinoma of the tongue can be staged according to the TNM staging defined as follows- (AJCC)

PRIMARY TUMOR (T)

T_X	Primary tumor cannot be assessed
T_0	No evidence of primary tumor
Tis	Carcinoma in situ
T_1	Tumor 2cm or less in the greatest dimension with the induration
T_2	Tumor more than 2cm but not more than 4 cm
T_3	Tumor more than 4 cm

T_{4a}	Tumor invades into deep (extrinsic) muscles of tongue, other regions of oral cavity
T_{4b}	Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery.

REGIONAL LYMPH NODES (N)

N_X	Regional lymph nodes cannot be assessed
N_0	No regional lymph nodes metastasis
N_1	Single ipsilateral lymph node 3cm or less in size
N_{2a}	Single ipsilateral lymph node more than 3cm but not more than 6 cm
N_{2b}	Multiple ipsilateral lymph nodes, none more than 6 cm
N_{2c}	Bilateral or contralateral lymph nodes, none more than 6 cm
N_3	Lymph node more than 6 cm

DISTANT METASTASIS (M)

M_X	Distant metastasis cannot be assessed
M_0	No distant metastasis
M_1	Distant metastasis

Stage				Disease free survival (Makitie, Koivunen et al. 2007)	
0	Tis	N_0	M_0	3 year	5 year
I	**T_1**	**N_0**	**M_0**	**88%**	**74%**
II	**T_2**	**N_0**	**M_0**	**74%**	**62%**
III	T_3	N_0	M_0	79%	61%
	$T_{1,2,3}$	N_1	M_0	79%	61%
IVA	T_{4a}	$N_{1,2}$	M_0	36%	33%
	$T_{1,2,3,4a}$	N_2	M_0	36%	33%
IVB	Any T	N_3	M_0	36%	33%
	T_{4b}	Any N	M_0	36%	33%
V	Any T	Any N	M_1		

Early cancer

The above highlighted stages; that is T_1, T_2 N_0 M_0 are the area of interest in this study. These stages are also defined as early carcinoma oral tongue in some studies.

The prognosis and survival of patients with squamous cell carcinoma of tongue changes depending upon the presence of lymph nodes metastasis. The 5 year survival is shown below: (Pillsbury 1997)

N_0 neck : 75%

N_1 neck : 49%

Two lymph nodes positive: 30%

Three or more lymph nodes positive: 13%

Occult lymph nodes

The prognostic significance of non-palpable (occult) metastasis in the N0 neck is less clearly defined. Studying this is more difficult because the T stage also affects prognosis and may overshadow the effect of occult neck nodes, and the final word on this is yet to be said.

The number of cervical lymph nodes histologically positive for squamous cell carcinoma provides the simplest, and perhaps most important, prognostic marker in carcinoma tongue (Beenken 1999). The control of locoregional recurrence solely depends on accurate diagnosis and treatment of the neck nodes (Hatta, Ogasawara et al. 1999; Kowalski and Sanabria 2007). The number of positive nodes clearly predicts risk for distant metastasic disease.

Mechanism of metastasis to lymph nodes in carcinoma oral tongue

The physiological function of the lymphatic system is to return interstitial fluid, plasma, and cells to the blood stream. Continuous contraction of the lymph vessels, compression of the interstitial tissue by the surrounding muscle allow passage of cells in the interstitium through clefts and into the lymphatic capillaries.

In the classical model, lymph flows from the capillaries through afferent vessels and into the marginal sinus in the cortex of the first echelon lymph node (sentinel lymph node). From the hilar efferent channels, lymph flows into the lymphatic trunks, joining lymph from neighboring groups of nodes. The valved lymphatic trunks then drain into the thoracic duct, subclavian and right lymphatic ducts.(Pillsbury 1997)

Lymph however does not always flow according to this classical model. It may completely bypass any intercurrent lymph node via pericapsular channels. The figure on

the left page depicts the lymph flow from the various regions of the tongue. The jugulodigastric node is the principal node (first echelon) of the tongue. There are some lymphatics, especially from the anterior of the tongue that drain directly to lower groups of lymph nodes without draining into the jugulodigastric nodes first.

The clinical significance of this observation is –

Presence of occult metastasis in level IV and level V cervical lymph nodes in the absence of metastasis in level I, II or III nodes. The significance of this is discussed and analyzed in detail.

Pattern of lymph node metastasis

The stage and pattern of lymph node metastasis to levels IV and V of cervical lymph nodes in the carcinoma of oral tongue has been found to be as follows according to various studies:

Author	Date	Stage	Number	Level	Skip mets
Lindberg (Lindberg 1972)	1972	T_1= 14% T_2= 30% T_3= 47.5% T_4= 76.55	-	overall	-
Byers (Byers 1986)	1986	T_{1-2}= 18.6% T_{3-4}= 31.6%	-	overall	-
Byers (Byers 1997)	1997	T_{1-4}	270	Level IV 15.8%	4.8%
Beenken (Beenken 1999)	1999	T_{1-2}	138	Level IV 1.4% Level V 0.7%	
Kaya (Kaya 2001)	2001	T_{1-4}	58	Level IV 2.8%	

Khafif (Khafif 2001)	2001	T_{1-3}	51	Level IV 2%	
Fernando (Fernando L. Dias 2006)	**2006**	**T_{1-2}**	**339**	**Level IV 0.5%**	**1.5%**

The overall incidence of metastasis in the different neck nodes levels is as follows:

Level

IA 3.3%

IB 22.8%

II 59.4%

III 10.4%

IV 2.6%

V 1.5%

Neck Dissections

There are various types of neck dissections employed for the treatment of N0 neck in early carcinoma tongue. The American Head and Neck Society and the American Academy of Otolaryngology has classified the various types of neck dissections and revised in 2001:

1991 classification	**2001 classification**
1. Radical neck dissection	1.Radical neck dissection
2. Modified radical neck dissection	2.Modified radical neck dissection
3. Selective neck dissection	3. Selective neck dissection(SND)
a. supraomohyoid	a. SND (Ia,Ib,IIa,IIb,III/IV)
b. lateral	b. SND (II-IV)
c. posterolateral	c. SND (II-V, postauricular,

	suboccipital)
d. anterior	d. SND (level VI)
4.Extended neck dissection	4. Extended neck dissection

1. Radical neck dissection consists of removal of all five lymph node groups on one side of the neck, including the sternomastoid muscle, the internal jugular vein and the spinal accessory nerve.

2. Modified radical neck dissections were developed with the intention of reducing the morbidity of the above operation by preserving:

Medina classification of MRND

MRND Type I – spinal accessory nerve preserved

MRND Type II – internal jugular vein and spinal accessory nerve preserved

MRND Type III – sternomastoid muscle, IJV and spinal accessory nerve preserved

3. Selective neck dissection consists of removal of only lymph node groups that are at highest risk of containing metastasis, according to the location of the primary.

4. Extended neck dissection also removes LN groups or structures which are not traditionally included in RND.

Current management of $T_{1-2}N_0$ neck

Treatment of N_0 neck is considered warranted when the probability of occult metastases is greater than 20% (Keski-Santti, Atula et al. 2006). Although it is well known that patients with advanced carcinoma tongue have a high risk of lymph nodal metastases, even those with early stage primary cancers, the extent of nodal involvement for each neck level remains controversial. This is mainly because of the heterogeneous nature of patient population in various study models, including several intraoral sites and different

T stages(Byers 1985; Shah 1990; Spiro 1996; Byers 1997; Fernando L. Dias 2006; Kowalski and Sanabria 2007).

The treatment options available are Modified radical neck dissection or a Selective neck dissection (Level I-III/IV). The rationale for selective neck dissection would be primarily based on predictable pattern of lymphatic spread associated with cancer of tongue as well of relative risk of lymph node metastasis (Ferlito, Rinaldo et al. 2006). Hence, the importance of determining the incidence of occult lymph node metastasis in early carcinoma tongue.

To date there have been various studies looking at the pattern of occult lymph nodal metastasis but these have been mostly retrospective and based on a mixed population of patients:

Fernando et al 2006 (tongue and floor of mouth primary)

Level	T_1 n=20	T_2 n= 62
I	12.2%	9.8%
II	13%	25%
III	1.7%	3%
IV	0.8%	0.8%
V	0	0

As shown in the above table in both T_1 and T_2 lesions the incidence of the occult metastasis to level II lymph nodes is the highest and that to level IV and level V is 0.8% and 0 % respectively in this series.

The current standard of care in India is variable and at our centre MRND for the neck and a wide local excision of the primary tumor on the tongue is offered to the patient. This is based on the principal that a neck dissection is warranted if the incidence of occult metastasis to neck would exceed 20 %(Lim, Lee et al. 2006). There is little data from the Indian population addressing the pattern of occult lymph node metastasis in this group of patients with T_{1-2} tumors of the tongue (Iype, Sebastian et al. 2008).

Morbidity associated with modified radical neck dissection in this group of patients

Scapular destabilization- the most troublesome sequelae after RND results from the removal of the spinal accessory nerve and denervation of the trapezius muscle. The resultant destabilization of the scapula leads to drooping, lateral and anterior rotation followed by progressive flaring of scapula. With modified radical neck dissection there is varying degrees of shoulder dysfunction due to extensive dissection around the spinal accessory nerve as required for level V and level IIb lymph nodal dissection(Kowalski and Sanabria 2007).

Chyle leak- another troublesome problem associated with modified radical neck dissection is a risk of chyle leak as a result of dissection of the level IV lymph nodes. Though the incidence of this complication is small, when chyle leak occurs it is a major complication requiring long postoperative hospital stay and probably a second operation.

Dissection of all the levels of lymph nodes is therefore not without its attendant morbidity(Callery, Spiro et al. 1984),and a selective neck dissection could avoid such potential morbidity(Iype, Sebastian et al. 2008).

Prognosis and Prognostic factors in early carcinoma tongue

The treatment of the neck in T_{1-2} N_0 carcinoma tongue requires accurate risk stratification to determine the type and extent of therapy needed and the expected clinical outcome. In addition to the TNM staging, other clinical and pathological factors not routinely incorporated into the staging system have been shown to influence response to therapy and outcome. The factors may be characterized as follows:

1. Prognostic factors related to the primary tumor
2. Prognostic factors related to cervical lymph nodes
3. Prognostic factors related to patient demographics

1.Tumor factors

Tumor dimensions

The T - stage takes into account the maximum visible/palpable tumor dimension. Because tumors arising from mucosal surfaces do not conform to spherical geometry, the maximal tumor diameter does not perfectly correlate with either tumor depth or tumor volume. The use of depth of tumor on pathological examination of the primary tumor has been seen so correlate well with incidence of occult metastasis to cervical lymphnodes(Fakih, Rao et al. 1989). Patients with a tumor depth of less than 4 mm were more likely to have uninvolved nodes at elective radical neck dissection compared with those with a tumor depth of greater than 4 mm(Fakih, Rao et al. 1989; Anthony Sparano MD 2004).

Primary tumor grading

Pathologists have long recognized the potential prognosis significance of cellular morphology in squamous cell carcinoma of tongue. Various grading systems have been used since 1920.

Most of them include the following factors (Bryne et al):

1. Degree of keratinizaiton- score of 1 to 4
2. Nuclear polymorphism-
3. Number of mitosis per high power field
4. Pattern of growth – invasive versus pushing
5. Angiolymphatic invasion

In addition to the malignancy grading studies have attempted to determine which individual histological parameters contribute strongly to prognosis. In a study of 45 patients with clinically N0 neck these various factors were assessed as being predictors of occult lymph nodal metastasis(Anthony Sparano MD 2004). The factors identified were

—

Greater tumor depth

Perineural invasion

Invasive growing front of the primary tumor

Poorly differentiated grade of the tumor

Perineural space invasion

Infiltration of perineural spaces occur in up to 52% of head and neck squamous cell carcinomas and was first noticed to influence surgical and adjuvant treatment strategies in 1963. Perineural invasion may result in dysphagia secondary to involvement of vagal trunk, or pain and hyperesthesia along the territories of the glossopharyngeal or trigeminal nerves. This perineural invasion may be mediated by the presence of nerve cell adhesion molecule (NCAM) on the surface of carcinoma, which engages in hemophilic binding with NCAM expressed in neural and perineural tissues. Numerous studies have associated the presence of perineural invasion with poor prognosis, but does the presence of perineural invasion correlate with the presence of occult metastasis to the neck nodes? It has been well established that there is a higher risk of loco-regional recurrence in the presence of perineural invasion in the primary tumor. This association between perineural invasion and local recurrence may result from centrifugal or centripetal propagation of malignant cells along the perineural space. As a result some malignant cells may even evade surgical excision. In addition, the association between perineural invasion and regional recurrence may imply that the tumor may be more aggressive(Anthony Sparano MD 2004).

Angiolymphatic invasion

One additional histological parameter not considered in traditional malignancy grading is vascular invasion; the presence of neoplastic epithelium within an endothelial – lined channel. This finding occurs in more than 50 % of specimens. As with other histological features, the presence of vascular invasion may identify tumors with an aggressive

biologic nature due to their ability to invade normal anatomic structures (Anthony Sparano MD 2004).

Invasive growing front of the primary tumor

The growing front of the tumor can be described at histopathological examination as a pushing front or an invasive front. It has been postulated that an invasive front predicts a more aggressive nature of the tumor. In 1989 Bryne et al proposed a model for grading of squamous cell carcinoma of head and neck. The pattern of invasion was considered in this model. The growing front could be scored :

1- pushing, well delineated infiltrating borders.

2- infiltrating, solid cords, bands, or strands.

3- small groups or cords of infiltrating cells.

4- marked and widespread cellular dissociation in small groups or in single cells.

Poorly differentiated grade of the tumor

As with most other squamous cell carcinoma, poorly differentiated grade of tumor in carcinoma tongue has been associated with aggressive nature of tumor.

2.Cervical lymph node factors

Number of positive lymph nodes on pathological examination

The number of cervical lymph nodes histologically positive for squamous cell carcinoma provides the simplest, and perhaps most important, prognostic marker in carcinoma tongue(Beenken 1999). The control of locoregional recurrence solely depends on accurate diagnosis and treatment of the neck nodes(Hatta, Ogasawara et al. 1999; Kowalski and Sanabria 2007). The number of positive nodes clearly predicts risk for distant metastasic disease.

Extracapsular invasion in the lymph node

Extracapsular invasion occurs in approximately 60% of patients with positive cervical nodes. The extent of extracapsular invasion can be stratified according to –

1. Macroscopic extracapsular spread with involvement of adjacent anatomic structures .
2. Macroscopic extracapsular spread confined to the perinodal fibro-adipose tissue.
3. Microscopic extracapsular spread.

It is a significant determinant of prognosis due to its association with increased risk of recurrence in the neck and distant metastatic disease.

Literature search did not reveal any prospective study done on Indian patients looking at $T_{1-2}N_0$ lesion of the tongue and assessing these factors.

MATERIALS AND METHODS

This was a descriptive study and was conducted in the Department of General Surgery – at the Christian Medical College and Hospital, Vellore from the 7th July 2006 to 15th August 2008 after obtaining appropriate approval from the Institutional Review Board of the hospital.

METHODOLOGY

Patients who were histologically confirmed to have carcinoma tongue, clinically T_{1-2} N_0 M_0 were recruited from the out patient clinic of the surgery department and approached for enrollment. Informed consent was obtained from these patients for inclusion in the study.

A detailed history was taken according to the study; clinical examination was carried out and recorded in a standard manner in the study Proforma. A "Head and neck examination diagram sheet" was used to map out the tongue tumors. All the patients underwent surgery for the primary tumor with either primary closure of the defect or reconstruction with a microvascular free forearm flap and a modified radical neck dissection within one week of examination. The exact dimensions of the primary tumor were mapped again at the time of surgery. The neck dissection specimen was marked and labeled in the theatre by the operating surgeon (level Ia, level Ib, level IIa, level IIb, level III, level IV, level V) using plastic markers and was taken to the pathology department for evaluation. The intra-operative details were noted in the patient Proforma. The duration of the operation was recorded. The pathology specimen was examined to evaluate for the primary tumor characteristics and the pattern of lymph node

metastasis by the pathologist. The tumor depth, the depth of muscle invasion was measured using calipers fixed on the microscope.

The patient underwent repeated examinations in the ward during the post-operative period to assess for post-operative morbidity related to the neck dissection, by using the "Constant's shoulder scale" on the 7th post-operative day. The morbidity related to the dissection around the spinal accessory nerve in the posterior triangle was assessed. Score was given from 100. The patient was also assessed for healing of the neck wound and appearance of any significant fluid in the drain.

A univariant analysis was done using SPSS software chi square test and p value of <0.05 was considered significant.

Inclusion criteria-

- Histologically proven carcinoma tongue, clinically $T_{1-2}\,N_0\,M_0$.
- No previous surgery, radiotherapy, or chemotherapy for the same.

Exclusion criteria-.

- Medically unfit for surgery.
- Not willing to take part in the study.
- Central location of the primary tumor on the tongue.

SAMPLE SIZE CALCULATION:

The literature search revealed the incidence of occult cervical lymph node metastasis to be 13-33% in a T1 lesion and 37-53% in T2 lesion. (30)

Taking the expected proportion of occult metastasis in the N 0 neck as 20 % and an absolute precision of 11 % at an alpha level of 5%, the sample size was calculated to be 51.

RESULTS

During the period of the study, from July 2006 to July 2008, **30** patients who were diagnosed to have early carcinoma tongue, clinically $T_{1,2}$ N_0 M_0, fulfilled the inclusion criteria of the study and were included in the study.

DEMOGRAPHY:

Sex Distribution

Figure 5

There were 17 (56.7%) males and 11 (43.3%) females.

Age

Figure 6

The age ranged from 25 years to 67 years with a mean age of 49 years.

Occupation

Figure 7

One patient was student, fourteen patients were unemployed and most of these were house wives.

Place of Residence

Figure 8

The majority of patients presenting to CMC-Vellore were from Tamil Nadu and West Bengal.

Socioeconomic status

Figure 9

The majority of the patients belonged to the middle socioeconomic class while two patients came from low socioeconomic status.

Duration of symptoms prior to diagnosis of cancer

Figure 10

The duration of appearance of the lesion and other symptoms prior to biopsy proven diagnosis of carcinoma tongue ranged from a 15 days to 50 months with a mean of 9.5 months.

Presence of risk factors

RISK FACTOR	Positive in nos of patients	Percentage
Sharp teeth	14	46.7
Oral tobacco	12	40
Smoking	9	30
Poor oral hygiene	7	23.3
Alcohol	5	16.7
Poor nutrition	2	6.7
Carious teeth	1	3.3

Table 1

The risk factors are listed in decreasing order.

Number of risk factors Figure11

This figure shows number of risk factors patients had. One patient presented without any identifiable risk factor. Eleven patients had a single risk factor while 5 patients had 2 risk factors. In 13 patients three or more risk factors were present at the time of diagnosis.

Presence of symptoms

Symptom	Present in number of patients	Percentage
Ulcer	30	100
Pain	19	63.3
Discomfort	10	33.3
Increased salivation	9	30
Difficulty in eating	8	26.7
Burning	7	23.3
Bleeding	4	13.3
Difficulty in speaking	3	10

Table 2

The symptoms are listed in decreasing order.

TUMOR CHARACTERISTICS AT PRESENTATION Figure 12

At presentation, 60 % of patients were found to have a T_2 N_0 M_0 lesion and 40 percent had a T_1 N_0 M_0 lesion.

Location of the tongue lesion Figure 13

The majority of patients had the ulcer at the lateral border of the tongue, one patient presented with ulcer on the dorsum of the tongue.

Side of the tongue lesion Figure 14

The majority of the ulcers were presented on the right side.

Size of the primary lesion in mm Figure 15

The length of the tongue lesion including the induration measured between 5 mm and 40 mm with a mean of 24.9 mm. There were 12 patients with lesion up to 20 mm (T1) and 18 patients with lesion measuring more than 20 mm and up to 40 mm (T2). None of the lesions crossed the midline.

Distance of the ulcer from the midline Figure 16

The mean distance of the lesion measured from the midline was 27.4 mm.

Distance of the lesion from the tip of the tongue Figure 17

The distance of the ulcer from the tip of the tongue was measured and ranged from 10 mm to 60 mm with a mean of 31.1 mm. Most of the tumors were located around 20 – 40 mm from the tip of the tongue.

OPERATION DETAILS

SURGERY (PRIMARY)	NO OF PATIENTS	PERCENTAGE
WLE tongue ulcer	23	76.7
Hemiglossectomy	7	23.3

Table 3

SURGERY (NECK)	NO OF PATIENTS	PERCENTAGE
MRND 1	3	10
MRND 3	27	90

Table 4

Three quarters (23) of patients underwent wide local excision, one fourth (7) underwent a hemiglossectomy. Four patients underwent reconstruction with microvascular free forearm flap following the hemiglossectomy. Three patients underwent an modified radical neck dissection type 1 based on suspicion of extracapsular lymph nodal disease. The rest of the patients underwent a standard a modified radical neck dissection type 3.

Intraoperative time Figure 18

The duration of surgery for the four patients who underwent free forearm micro vascular flap was 11, 12, 15, 17 hours respectively. For the rest of the patients, duration of surgery ranged from 2 hours 30 minutes to 5 hours 30 minutes. **The overall mean duration of surgery was 4hours excluding reconstruction.**

HISTOPATHOLOGICAL DETAILS

Number of occult lymph node positivity in the patients Figure 19

Out of 30 patients who underwent neck dissection 76.6 % (n = 23) of patient were confirmed to be histologically N_0. The overall percentage of occult metastasis was found to be **23.3 percent (n = 7)** among these patients. The percentage of patients with pN_1 disease was **10 percent** (n = 3), that of pN_{2a} was **0 ,** that of was **13.3 percent** (n = 4).

The levels of lymph nodes involved with occult metastases were analysed. The pathological details of the occult metastases are described below:

Number of patients with positive occult lymph nodal metastasis at specific level of lymphnodes.

Level LN	Number (%) (n = 30)
Ia	1(3.3)
Ib	0
IIa	4(13.3)
IIb	2(6.7)
III	1(3.3)
IV	0
V	0

Table 5

The first echelon lymph node (i.e. level IIa) had the maximum number of occult metastasis.

Details of lymph node level metastasis in each of the seven patients with occult mets

Patient number	occult mets
1st	IIa only
2nd	IIa and IIb
3rd	III only
4th	IIb only
5th	IIa only
6th	Ia only
7th	IIa only

Table 6

This table shows the pattern of occult nodal metastasis in each patient.

Clinical T staging versus occult lymph node positivity Figure 20

TN stage	Number of patients	Number of patients pN negative	Number of patients pN positive
T1	12 (40%)	10 (83.3%)	2 (16.7%)
T2	18 (60%)	13 (72%)	5 (28%)

Table 7 **p value 0.669**

The above table 7 shows the percentage of occult lymph node positivity in T_1 versus T_2 patients. There were 12 patients with T_1 (primary lesion less than up to 2 cm) and 18 patients with T_2 (primary lesion more than 2 cm up to 4 cm).

Mean size of primary tumor in occult lymph node positive patients

Occult lymph nodes	Mean length of primary tumor
Negative (23)	23.6 mm
Positive (7)	29 mm

Table 8 **p value 0.217**

The p value was not significant.

Mean depth of primary tumor in occult lymph node positive patients

Occult lymph nodes	Mean depth of primary tumor
Negative (23)	4.6 mm
Positive (7)	6.4 mm

Table 9 **p value 0.167**

Depth of primary lesion	Number of patients	percentage	p N negative (%)	p N positive (%)
<= 2mm	8	26.7	7 (87.5%)	1 (12.5%)
2-4 mm	6	20	4 (66.7%)	2 (33.3%)
>= 4 mm	16	53.3	12 (75%)	4 (25%)

Table 10 **p value 0.642**

The mean depth of primary tumor on histopathological analysis was 4.6mm for pN negative patients and 6.4mm for pN positive patients. This difference was not found to be statistically significant.

Mean depth of muscle invasion in occult lymph node positive patients

Occult lymph nodes	Mean depth of muscle invasion in primary tumor
Negative (23)	3.1 mm
Positive (7)	5.0 mm

Table 11 **p value 0.096**

Depth of muscle inv	Number	%	p N negative	p N positive
<= 2mm	15	50	13 (86.7%)	2 (13.3%)
2-4 mm	4	13.3	3 (75%%)	1 (25%)
>= 4 mm	11	36.7	7 (63.7%)	4 (36.3%)

Table 12 **p value 0.389**

The mean depth of muscle invasion on histopathological analysis was 3.1mm for pN negative patients and 5.0mm for pN positive patients.

Perineural invasion Figure 21

This figure shows the percentage of presence of perineural invasion in all the primary tumor specimens was 36.3%.

Table 13 shows that all the patients who were found to have occult lymph nodal metastasis had perineural invasion in the primary tumor and none of the patients with pathologically negative nodes did.

p N (nos of patients)	Perineural invasion present	Perineural invasion absent
Potitive (7)	7 (100%)	0
Negative (23)	0 (100%)	23 (100%)

Table 13 **p value 0.000**

Angiolymphatic invasion Figure 22

The figure 22 shows the percentage of specimens demonstrating angiolymphatic invasion in the primary tumor was 30 %.

p N (nos of patients)	Angiolymphatic invasion present	Angiolymphatic invasion absent
Positive (7)	6 (85%)	1 (15%)
Negative (23)	3 (13%)	20 (87%)

Table 14 **p value 0.001**

Among the patients with occult lymph nodal metastasis 85% of the patients had angiolymphatic invasion, as compared to 13% of patients with no occult lymph nodal metastasis.

Pushing front versus invading front

p N (nos of patients)	Pushing front (n =16) 53.35%	Invading front (n =14) 46.6%
Positive (7)	1 (14.2%)	6 (85.7%)
Negative (23)	22 (95.6%)	1 (4.3%)

Table 15 **p value 0.031**

85.7% of patients had invading front of the primary tumor among the pN positive patients versus 4.3% of patients among pN negative patients.

Patient characteristics and occult lymph node positivity

Primary tumor charcteristics	Number Total = 30	percentage	p N negative	p N positive	p value
Oral tobacco					
Yes	12	40	10 (83.3%)	2 (16.7%)	0.669
No	18	60	13 (72.2%)	5 (27.8%)	
Smoking					
Yes	9	30	7 (77.8%)	2 (22.2%)	1.00
No	21	70	16 (76.2 %)	5 (23.8%)	
Alcohol					
Yes	5	16.7	4 (80%)	1 (20%)	1.00
No	25	83.3	19 (76%)	6 (24%)	
Sharp teeth					
Yes	14	46.7	12 (85.7%)	2 (14.3%)	0.399
No	16	53.3	11 (69%)	5 (31%)	
SES					
Low	2	6.6	2 (100%)	0	0.715
Medium	23	76.6	17 (74%)	6 (26%)	
High	5	16.6	4 (80%)	1 (20%)	
Duration of symp					
< 6 months	17	56.7	11 (64.7%)	6 (35.3%)	0.104
>6 months	13	43.3	12 (92.3%)	1 (7.7%)	
GRADE					
Well differentiated	10	33.3	8 (80%)	2 (20%)	0.140
Moderately diff	20	66.7	15 (75%)	5 (25%)	
Poorly diff	0	0	-	-	

Table 16

POST OPERATIVE MORBIDITY

Duration of postoperative stay Figure 23

The mean duration of postoperative stay was 7.2 days. The four patients who underwent micro vascular flap reconstruction had a longer postoperative stay. The mean duration of postoperative stay for these patients was 15 days.

There was no wound or drain related morbidity in any of the patients. None of the patients had prolonged wound drainage in the drain and none had chyle leak.

The mean number of days requiring wound neck drain was 5.4 days.

Constant's Scale score for shoulder dysfunction at 7 post-op days Figure 24

The maximum Constant's Scale score is 100. On the seventh postoperative day shoulder dysfunction was measured. The mean score using this scale was 58.3. The highest score was 67.5 and lowest being 45.0.

DISCUSSION

Demographic details of the patients

In this study a total of 30 patients with either T_1 or T_2, N_0 squamous cell carcinoma of the tongue were analysed. The male to female ratio was nearly equal 56.7% versus 43.3% and the mean age of these patients was 49 years, (median age 45 years) ranging from 25 years to 67 years. The male to female ratio for incidence of oral malignancy has been equal throughout the world. The median age has been found to be around 45 years in various studies with a recent trend of increasing incidence among the younger age group(Shiboski, Schmidt et al. 2005). Most of these patients belonged to the middle socioeconomic status.

The patients presented from both South India and North India. This has little to do with the distribution of the disease, but reflects the trend of patient population in our hospital. Mean duration of symptoms prior to making diagnosis of carcinoma tongue at CMC-Vellore was 9.5 months with a median of 5 months (range from 15 days to as long as 50 months).

Clinical details of the patients

All the patients presented with symptom of ulcer and a large number complained of pain at the ulcer site. Other symptoms of discomfort, increased salivation, difficulty in eating and burning were present in much less number of patients. The presence of various defined risk factors were analysed in this series of patients and it was found that the most common single risk factor identified was presence of sharp teeth (46.7%). Presence of stained teeth or oral tobacco also were also found to be very high - 43.3 %. The majority of patients were identified to have multiple risk factors.

About 30% of tobacco grown in India goes into cigarette production, but *Bidi* is the most popular form of tobacco use in India. About 34% of the tobacco produced in India is used for the manufacture of *Bidis*. They contain small amount of coarsely ground tobacco as compared to more amount of finely cut tobacco in cigarettes. Yet, *bidi*s deliver more tar than the cigarette. As *Bidi* is cheaper it is used more commonly.

Use of oral tobacco is in the form of *Pan* (betel squid) with tobacco. *Pan* consists of four main ingredients: betel leaf (*Piper betle*), areca nut (*Areca catechu*), slaked lime and catechu (*Acacia catechu*). In addition to tobacco, areca nut affects the oral health as it releases powerful nitrosamines, proven to be carcinogenic in animal models.

The number of patients with T_1 to T_2 lesions were 12 and 18 respectively. All but one tumor were situated on the lateral border of the tongue. Lateral border of the tongue is more prone to carcinogenesis due to pooling of carcinogen laden saliva in the floor of the mouth. It was also found that the 60% of the lesions were on the right side and 40% on the left side. The significance of this is not known. Literature review failed to reveal any significance of this finding. The tumor was mapped on the tongue and it was found that most of the ulcers were situated between 20 and 40 mm from the tip of the tongue. This is the area of the upper 2nd premolar tooth.

For the primary either a wide local excision was done or a hemoglossectomy was performed. Seven patients underwent hemoglossectomy. All patients had MRND for the management of neck. None of the patients had RND. Three patients had an MRND 1 based on suspicion of extracapsular lymph nodal disease. The mean duration of the operation was 4 hours 30 minutes.

Histopathological examination of the neck dissection specimens

On pathological examination of the neck dissection specimens among all the 30 patients a total of 7 patients (23.3%) were found to have occult metastasis in the lymph nodes upstaging the disease from N_0 neck to N_1/N_2 neck -- 10% of patients were upstaged to pN_1 and 13.3% to pN_2.

In a European study published in 2007 on analysis of retrospective cohorts of patients with various stages of carcinoma tongue, the 3- and 5-year disease free survival rates were: Stage I, 88% and 74%; Stage II, 74% and 62%; Stage III, 79% and 71% and Stage IV, 36% and 33%. (Makitie, Koivunen et al. 2007). These observations suggest that MRND operation may help in prognosticating the disease in a subset of patients.

Assessment of the pattern of lymph nodal occult metastasis also revealed the metastasis were found at -- level I 3.3%, level IIa 13.3%, level IIb 6.7%, level III 3.3%, level IV, V 0%. These results were compared with other studies --

Study done in 2004 by Anthony(Anthony Sparano MD 2004) on 45 patients diagnosed to have T_{1-2} N_0 carcinoma tongue were assessed and 28.9% of the patients were found to have occult lymph nodal metastasis with the highest incidence being at the level IIa lymph nodes. Another study done in 2006 by Fernando(Fernando L. Dias 2006) 121 patients with T_{1-2} N_0 carcinoma tongue were assessed and 46% of the patients were found to have occult metastasis, the highest incidence being at level II lymph nodes. The

difference is probably because of different patient populations and also the sample size has not been completed in the present study.

Several clinical and pathological studies have demonstrated that the pattern of metastatic lymph node metastases occurs in a predictable fashion in patients with oral and oropharyngeal carcinoma.(Kowalski and Sanabria 2007). For carcinoma tongue the first echelon lymph nodes to get involved seem to be levels I, II or III depending on the site of the tumor on the tongue. The involvement of levels IV and V seems to be rare, and isolated involvement of levels IV and V without involvement of levels I, II or III, that is , **skip metastasis**, seems to be rarer(Lindberg 1972). Various studies have cited different percentages of skip metastases to these levels:

Shah et al have reported the skip metastatis rate as1.5% (Shah 1990), Byers et al have reported 4.8%(Byers 1997), Beenken et al have reported 0.7%(Beenken 1999), Kaya et al have reported 2.8%(Kaya 2001), Khafif et al have reported 2%(Khafif 2001) and Fernando et al have reported 1.5%(Fernando L. Dias 2006).

Presence of skip metastasis is one of the reasons to recommend an MRND III for a patient with early carcinoma tongue with clinically negative neck.

On the contrary, the rationale for a selective neck dissection is primarily based on predictable pattern of lymphatic spread associated with cancer of the tongue as well as the relative risk of lymph node metastasis to the various levels of lymph nodes (Ferlito,

Rinaldo et al. 2006). A number of anatomic, radiographic, pathologic and clinical studies have demonstrated that lymphatic drainage of the cancers of head and neck follow predictable routes of spread (Lindberg 1972; Ferlito, Rinaldo et al. 2006). In 1972, Lindberg's clinical study(Lindberg 1972) demonstrated the jugulodigastric and mid jugular groups of nodes, levels II and III, respectively, to be the most frequently involved in metastatic spread from primary carcinomas of the tongue. He also pointed out the occasional propensity of metastatic spread from these primary tumors to skip first echelon nodes and metastasize directly to the mid-jugular (level III) group of nodes. Nevertheless, in the absence of disease in the levels I and II, involvement of the low jugular and posterior triangle nodes, level IV and V, is exceedingly rare(Lindberg 1972).

In 1990, Shah(Shah 1990), in a retrospective study of 1119 RND specimens, demonstrated that primary carcinomas of oral cavity most characteristically metastasized to lymph node levels I, II and III. An even more important aspect of this study was that when node levels I-IV were negative, level V was never node positive. This is the basic reason for the concept of Selective neck dissection in the management of N_0 neck in the early carcinoma of the tongue.

Risk stratification and prognostication based on characteristics of the primary tumor on the tongue

The risk of cervical metastasis depends upon numerous clinicopathological factors, T-stage, site, microscopic pattern of invasion, lymphovascular invasion, and thickness of the tumor(Smith 2004).

Size of primary

The mean largest diameter of the primary tumor in patients with pN positive disease was 29 mm and that in pN negative disease was 23.6 mm. This difference was not found to be statistically significant as the p value was 0.217. Other studies also had similar finding. The current staging define T stage using length and breadth of the tongue lesion unlike other gastrointestinal mucosal malignancies for which depth is considered in the T stage. As the cancer of the tongue grows in the three dimensions the visible largest dimension may not be the most important factor important for prognosis. The mean depth of primary tumor in patients with pN positive disease was 6.4 mm as compared to 4.6 mm in pN negative disease. This difference was not found to be significant. G.I.Smith et al have suggested to take 4 mm as cut off for higher chance of occult metastasis, thereby recommending elective neck dissection for patients with oral tongue cancers that are 4mm or more thick(Smith 2004). Anthony in 2004 study (Anthony Sparano MD 2004), also showed a significantly higher incidence of occult nodal metastasis in the presence of tumor thickness more than 4mm.

Perineural invasion

Presence of perineural invasion has been reported in literature to widely vary form 5% to 95%. In this study perineural invasion was present in 36.3% of patients. In another study(Anthony Sparano MD 2004) published in 2004 on American population based patients it was found to be 33.3%. In this study perineural invasion in the primary tumor was not seen in any patient with pN negative disease and was seen in 63.6% of patients with pN positive disease. This difference was found to be statistically significant (p value 0.000). This finding is very important in the context of this discussion. From the finding of this study it may be summarily stated that if a patient does not have perineural invasion in the primary tumor, the chance of having occult nodal metastasis is extremely low, which is keeping with already established views.(Anthony 2004).

Angiolymphatic invasion

Presence of angiolymphatic invasion in this study was 30%. This percentage was 85% among the node positive patients and 13% among the node negative patients. Also if angiolymphatic invasion was found then 66.5% patients were found to be node positive and if invasion was angiolymphatic negative then only 4.8% patients were found to be node positive. This difference was statistically significant. This finding has been supported by various studies (Fakih, Rao et al. 1989; Anthony Sparano MD 2004).

Tumor growing front

Among the node positive patients, 85.7% of the patients had an invading front of the primary tumor, this percentage being 4.3% in node negative patients. This difference was found to be statistically significant. This finding has been supported by various studies (Fakih, Rao et al. 1989; Anthony Sparano MD 2004).

Grading

Though there was no difference in node positivity according to the over all grading (well, moderate and poorly differentiated). In a study by Anthony(2004)(Anthony Sparano MD 2004), poor tumor cell differentiation was found to be associated with occult node positivity and that was found to be statistically significant (p value of 0.007). On multivariate analysis infilterating growth front were found to have significance (Anthony Sparano MD 2004). The tumor cell grading , angiolymphatic invasion, tumor thickness, T stage were not associated significantly with occult node positivity(Anthony Sparano MD 2004).

In this study the factors which were found significantly associated with occult lymph nodal metastasis were:

1. Presence of perineural invasion in the primary tumor specimen.
2. Presence of angiolymphatic invasion in the primary tumor specimen.
3. Presence of infiltrating front in the primary tumor specimen.

Location

The location of the tumor on the tongue did not affect the pattern of lymph node metastasis. (p value 0.372). A higher sample size will be required to come to a conclusion.

Postoperative morbidity related to the neck dissection

The post operative morbidity related to the posterior neck dissection is mainly shoulder dysfunction arising due to dissection around the spinal accessory nerve. Constant's score was calculated for all the patients on the 7th postoperative day. The mean score was 58.3, the normal score being 100. This score was significantly low.

In another study (Laverick 2004) it was interesting to note the mean shoulder dysfunction scores were same in patients who underwent a level III/IV dissections and patients who did not undergo any neck dissection. Whereas patients with unilateral level V dissections reported much worse scores on average.

This added morbidity of shoulder dysfunction after neck dissection seems to be mainly due to level V dissections. In our group of patients the incidence of level V lymph node occult metastasis seems to be very small. It does not seem appropriate to expose every patient to this added morbidity in order to salvage a minor group of patients.

Concept of selective neck dissection versus a classical modified radical neck dissection in early carcinoma tongue

In 1998, Leemans and Snow(Leemans 1998) published a metaanalysis of 1179 patients reporting the results of elective selective neck dissection and MRND in treatment of clinically negative neck. From this retrospective survey they concluded that recurrence rates are higher in selective neck dissection than after MRND. This data lead to the conclusion that selective neck dissection was not acceptable.

On the other hand in 1998 study(group 1998) published by the Brazillian head and neck cancer study group compared SND I-III with MRND in a prospective manner in patients with oral cancer with clinically negative neck nodes. The regional control and overall 5 year survival were 87.5% and 67% for the SND group versus 89.5% and 63% for the MRND group. The differences were not statistically significant. The same group pubslished another study in 1999 (group 1999)comparing results of SND II-IV with MRND and found no difference between the two groups in terms of 5 year survival rates and regional control.

Therefore, a randomized controlled trials in single institution is necessary to confirm the role of selective neck dissection *vis-à-vis* modified radical neck dissection III in early carcinoma tongue patients with clinically negative neck nodes.

It has been pointed out that “the concept of treating all patient with a N0 neck with a modified radical neck dissection is analogous to shooting a rabbit with a shotgun rather than a rifle”(Ferlito, Rinaldo et al. 2006). If a selective neck dissection is used there is a little chance of a recurrence outside the dissected area. The low incidence of recurrences

may not justify a concept of treating all patients with MRND, however, it takes skill and experience to perform a selective neck dissection appropriately. This is because there are no set anatomical boundaries between the various lymph nodal levels.

The arguments in favor of a selective node dissection can be:

1. The predictable nodal spread for a given primary tumor.

2. The decreased morbidity.

3. Salvage after failure is possible.

The arguments against a selective neck dissection can be:

1. There are no anatomical boundaries between levels that have to be removed and that can be left behind.

2. There can be subjective sparing of non-lymphatic structures.

3. Direct spread to levels IV and V jugular lymph nodes does occur.

CONCLUSIONS

1. The lymph nodal occult metastasis occurs most commonly at levels I, II, and III in early carcinoma tongue with clinically negative neck. When there is minimal or no tumor at the level I, II or III lymph nodes in early carcinoma tongue, the likelihood of finding tumor at levels IV and V is low.

2. Presence of the following in the primary tumor significantly affects the presence of occult neck metastasis-

i. perineural invasion

ii. angiolymphatic invasion

iii. invasive tumor growing front

3. There is significant post operative morbidity after an MRND. A selective neck dissection may reduce the morbidity of this operation in early carcinoma tongue.

The study proves and supports the hypothesis –

A "comprehensive" (modified neck dissection III) neck dissection is not warranted in patients with clinically $T_{1\text{-}2}$ N_0 M_0 carcinoma tongue in the context of patients of Indian origin.

LIMITATIONS

1. The sample size could not be completed in the duration of the study time (24 months), further study is required to complete the sample size.

2. Some of the occult lymph nodal metastasis could have been missed and may require ultra thin sectioning of the lymph node specimens for more detailed pathological examination.

RECOMMENDATIONS

1. Selective neck dissection (levels I, II , III) for carcinoma tongue $T_{1-2}N_0M_0$ is perhaps an adequate operation. An MRND is not without its morbidities.

2. High risk patients can be identified based on the histopathological characteristics of the primary tumor; presence of perineural invasion, angiolymphatic invasion and invasive growth front and the management plan for each patient can be individualized.

3. Further studies may be necessary to look into issues of sentinel lymph node biopsy and for preoperative ultrasound evaluation for non palpable neck nodes.

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Patient information and Consent Form

Optimal management of the neck in an early carcinoma tongue.

Introduction

You are invited to take part voluntarily in a research study to determine the optimal management of the neck in an early carcinoma tongue. Before agreeing to participate in this research study, it is important that you read and understand this form. It describes the purposes, procedures, benefits, risks and discomforts of the study. It also describes alternate procedures that are available to you and your right to withdraw from the study at any time. If you participate in the study, you will receive a copy of this form to keep for your records.

Purpose of this study

The purposes of this study are—

1. To study the pattern of presence of cancer cells in the neck nodes, if any, in the surgical specimen after the surgery when you were not detected to have nodes in the neck nodes clinically.
2. To study the relationship, if any, between the above mentioned cancer cells in the neck nodes and the tongue tumor clinical and pathological characteristics. To be able to predict in future the pattern of cancer cells in the neck on evaluation of the primary tumor.
3. To look for any post-operative problems due to the comprehensive neck dissection.

Qualifications to participate

The doctor in charge of the study will discuss with you regarding the requirements for the participation in this study. It is important to be completely truthful about your health history. You should meet the following requirements to participate in this study—

1. Diagnosed to have early carcinoma tongue – stage I or stage II
2. Not taken any prior surgical treatment or radiotherapy or chemotherapy for the cancer.
3. Willing to undergo operative treatment in CMC Vellore for the cancer.
4. You must be willing to visit the doctor's office at request both during the active treatment and during the follow up.
5. You must sign this infirmed consent.

You cannot take part in the study if—

1. You have taken the foresaid treatment.
2. You are unwilling or not fit for the operation offered.

Study Procedures

If you agree to participate in the study the doctor will take a detailed history and conduct a physical examination. There are no extra blood tests required as part of the study. You will be offered the option of appropriate operation for your cancer. In this institution the appropriate operation offered for stage I or II carcinoma tongue is wide excision of the primary tumor tongue and a comprehensive neck dissection. If you agree to under go the operation a date for the surgery will be given to you. The operation will be performed in the usual standard way. The surgical specimen will be examined by the doctor in detail for which there will be no added cost to you. You will be examined by the study doctor in the post-operative period to look for any complications. You will be required to follow up in the hospital for few weeks post-operatively to be examined for any continuing morbidity.

Risks and discomforts associated with this study

As the doctor is proposing the standard care and operation for your disease; and does not offer any extra investigations, there are no risks associated with the study as such. But you ought to understand that any surgical procedure and anesthesia carries its own risks and complications. You should consent for the operation only after understanding those. These will be explained to you by the operating surgeon.

Other treatments

The literature suggests the current gold standard treatment of stage I or II carcinoma tongue is wide excision of the primary tumor tongue and a modified radical neck dissection. This will be offered to you as part of this study. The other options available are a less comprehensive neck dissection and radiotherapy. You do not have to be part of this study to be treated for your condition.

Participation in the study

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or may stop your stop your participation in the study at any time, without a penalty.

Signature

To become a part of the study, you or your legal representative is required to sign this page. By signing this page you are confirming the following:

- You have been explained all the information in this Patient Information and Consent form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.
- You voluntarily agree to be part of this research study, to follow study procedures, and provide necessary information to the doctor as required.
- You may freely choose to stop being part of this study at any time.
- You have received a copy of this Patient Information and Consent form to keep for yourself.

Patient name Patient hospital number

Signature of patient or legal representative Date and time

Name of the individual conduciting informed consent discussion

Signature of the individual conduciting informed consent discussion Date and time

THESIS PROFORMA

Study no:

I) DEMOGRAPHIC DETAILS---

Name: Age: yr Sex: M / F H. NO:

Occupation: Ht: cm Wt: kg

Resident of:

Extent of education:

1. uneducated 2.primary school 3.high school 4.undergraduate
5. postgraduate

Socioeconomic status:

II) EXPOSURE TO RISK FACTORS ---

1.oral tobacco 2.smoking 3.alcohol 4.teeth sharp 5.nutrition 6.others
Others—

III) TUMOR DETAILS ---

SYMPTOMS-

1.ulcer 2.discomfort 3. pain 4.increased salivation
5.difficulty in speaking 6.difficulty in eating 7.unsatisfacotry cosmetic 8.bleeding
9.burning

Time in months since initial symptoms:
Time in months before medical help sought:

Any previous treatment taken:

1.native practitioner 2.homeopathy 3.MBBS doctor 4.specialist

Details of previous treatment if any:

Time in months between initial symptoms and diagnosis of cancer:
Time in months between diagnosis of cancer and coming to Vellore:

ON EXAMINATION: Date:

Oral cavity:

1.normal 2.poor oral hygiene 3.stained teeth 4.carious teeth
5.sharp teeth

PRIMARY TUMOR:

Location:

1.lateral border 2.tip 3.dorsum 4.margin of tongue

Extent:

Does it cross midline:

1. yes 2. no

Distance of the medial border from midline: mm

Distance of anterior border from the tip of tongue: mm

Distance of posterior border from the posterior extent of oral tongue: mm

Size:

Of the visible lesion: mm X mm

Of the induration: mm X mm_

Surface:

1.ulcerative 2.fungating 3.verrucous 4. flat (infiltrative)

Other lesions:

1.normal 2.submucosal fibrosis 3.leukoplakia 4.erythtoplakia
5.second primary

If second primary, the site of the lesions and details:

EXAMINATION OF THE NECK:

1.Facial node present 2. Facial node absent 3.contralateral facial node present

No other neck nodes palpable: 1.yes 2.no

Other medical / surgical problems:

IV) TNM STAGING :

1. T1N0M0 2. T2N0M0

V) INVESTIGATIONS:

Hb : PCV :

Serum Creat:

Chest Xray:

Biopsy:

Date:
Grade:
1.well differentiated 2.moderately differentiated 3.poorly differtiated

Other investigations—

VI) OPERATION DONE: Date:

Primary:
1.wide local excision 2.hemiglossectomy

Neck:
1.MRND I 2.MRND II 3.MRND III 4.RND

Intra-operative findings:

PRIMARY:
Size: mmX mm
Extent:
Does it cross mid line:
1. yes 2. no
Does it extend into the post one-third of the tongue:
1.yes 2.no
Does it extend into the floor of the mouth:
1. yes 2.no
Does it involve the alveolus:
1.yes 2.no

LEVEL Ia
1. no LN
2. single LN
3. multiple LNs
exact number of LNs:
size of the largest LN:

LEVEL Ib:
1. no LN
2. single LN
3.multiple LNs
exact no of LNs:
size of largest LN:

LEVEL IIa:
1. no LN
2. single LN
3. multiple LNs
exact number of LNs:
size of the largest LN:

LEVEL IIb:
1. no LN
2. single LN
3. multiple LNs
exact number of LNs:
size of the largest LN:

LEVEL III:

1. no LN
2. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:

LEVEL IV:

1. no LN
2. sisingle LN
3. multiple LNs

exact number of LNs:
size of the largest LN:

LEVEL V:

1. no LN
2. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:

VII) POST-OPERATIVE MORBIDITY-

Intra-operative time: hrs minutes

Number of in patient days:

Flap necrosis:
1. no 2. minor 3.major

Wound infection:
1. no 2.minor 3.major

Wound discharge:
1. no 2.serous 3.pus 4.bloody

Wound drainage: Day 1 2 3 4 5 6 7
8 9 10 11 12 13 14

Drain removed on which post-op day:

Drain:
1. serous 2.lymphatic leak 3.chyle leak

Suture removal on which post-op day:

CONSTANTS SCALE FOR SHOULDER DYSFUNCTION:—

AT DAY 7 3 MONTHS

PAIN:

1.Severe_____
2.Moderate_____
3.Mild_____
4.None_____

ACTIVITY LEVEL

Sleep affected:

1.yes_____
2.sometimes_____
3.no_____

Recreation limitation:

1.severe_____
2.moderate_____
3.no_____

Daily activities limitations:

1.severe_____
2.moderate_____
3.no_____

Arm positioning:

1.up to the waist_____
2.up to xiphoid_____
3.up to neck_____
4.up to top of head_____
5.above head_____

Strength of Abduction:

1.nil_____
2.less than the opposite side_____
3.equal to the opposite side_____

RANGE OF MOTION

Forward flexion:

1.31-60 degrees_____
2.61-90 degrees_____
3.91-120 degrees_____
4.121-150 degrees_____
5.151-180 degrees_____

Lateral flexion:

1.31-60 degrees_____
2.61-90 degrees_____
3.91-120 degrees_____
4.121-150 degrees_____
5.151-180 degrees_____

External rotation:

1.hand behind head, elbow forward_____
2.hand behind head, elbow back_____
3.hand to top of head, elbow forward_____
4.hand to top of head, elbow back_____
5.full elevation_____

Internal rotation:

1.lateral thigh_____
2.buttock_____
3.lumbosacral junction_____
4.waist(L3) _____
5.T12 Vertebra_____
6.interscapular (T7) _____

_____
TOTAL SCORE—
_____

VIII) HPE REPORT:

PRIMARY:

a) Description:

1. uclerative 2.fungating 3.verrucous 4. flat (infiltrative)

b) Grade:

1. well differentiated 2.moderately differentiated 3.poorly differentiated

c) Size: mm X mm d) Depth of lesion (maximum): mm

e) Perineural invasion: f) Angiolymphatic invasion:

1. present 2.absent 1. present 2.absent

g) Growing front:

1. invasive 2.pushing

h) Depth of muscle invasion (maximum): mm

i) Margins:

1. free of tumor 2. involved

Which margin involved- Distance of tumor from the margins- mms

LYMPH NODES:

LEVEL Ia

1. no LN
3. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:
capsular invasion: 1. yes 2 no

LEVEL Ib:

1. no LN
2. single LN
3.multiple LNs

exact no of LNs:
size of largest LN:
capsular invasion: 1.yes 2.no

LEVEL IIa:

1. no LN
2. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:
capsular invasion: 1. yes 2. no

LEVEL IIb:

1. no LN
2. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:
capsular invasion:1.yes 2.no

LEVEL III:

1. no LN
2. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:
capsular invasion: 1. yes 2. no

LEVEL IV:

1. no LN
2. sisingle LN
3. multiple LNs

exact number of LNs:
size of the largest LN:
capsular invasion:1.yes 2.no

LEVEL V:

1. no LN
2. single LN
3. multiple LNs

exact number of LNs:
size of the largest LN:
capsular invasion: 1. yes 2. no

NECK:

1.N0 : no suspicious node

2.N1 : Single ipsilateral LN <3cm
Exact site:
Exact size:

3.N2:a- Single ipsilateral LN 3cm-6cm
Exact site:
Exact size:

4.N2:b- Multiple ipsilateral LNs all <6 cm
Number of nodes:
Exact sites:

Size of each node:

5.N3 : Any LN >6cm
Number of nodes:
Exact sites:

Size of each node:

IX) FOLLOW UP—

ORAL LESION:

Tongue wound:

1. healed well 2. not healed well 3.restiction of mobility
4.speech limitation 5.limitation in food intake

Second primary: 1. no 2. yes

If yes,

Description of the lesion:

Size
Type
Position

Recurrence: 1. no 2. yes

If yes,

Description of the lesion:

Size
Type
Position

NECK :

Any palpable lymph nodes :

SAME SIDE
1.No LNs 2. LN s palpable
What level:

CONTRALETRAL LNs
1.No LNs 2. LN s palpable
What level:

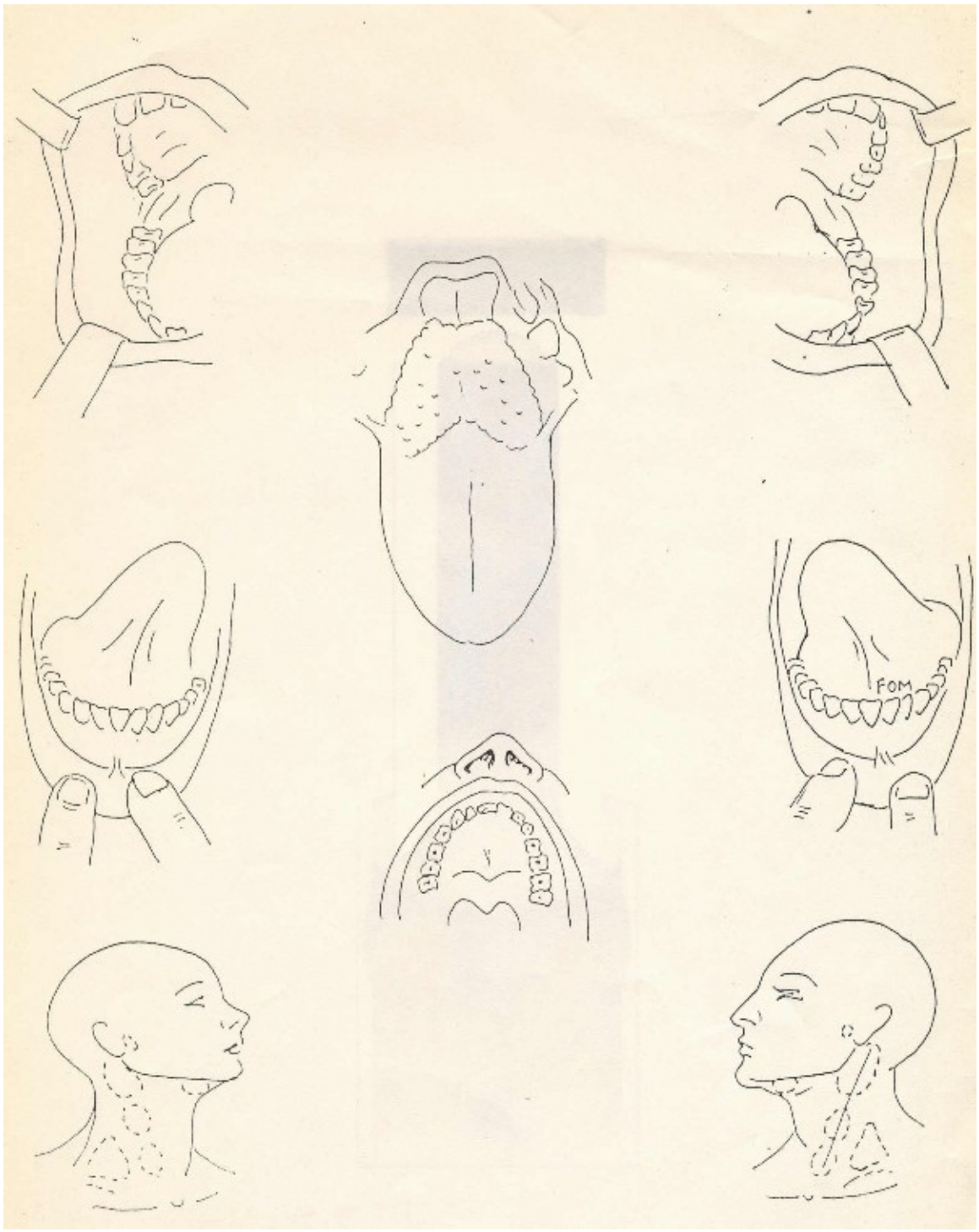
Wound:

1.healed with primary intention 2.healed with secondary intention

METASTASIS:

Chest Xray :

Other:


FOM